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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/756,125	01/12/2004	Dennis R. Burton	TSRI 882.1	3579

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EXAMINER	
CHEN, STACY BROWN	
ART UNIT	**PAPER NUMBER**
1648	

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12/21/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/756,125	BURTON ET AL.	
	Examiner	Art Unit	
	Stacy B. Chen	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *5/1/07; 7/26/07; 9/28/07*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *See Continuation Sheet* is/are pending in the application.

4a) Of the above claim(s) *11-14,30-33,49-52 and 68-71* is/are withdrawn from consideration.

5)☒ Claim(s) *1,2,9,15,19,20,22,28,38,39,41,47,53 and 57* is/are allowed.

6)☒ Claim(s) *16,17,29,34-36,54,55,58-60,66,72-74 and 76* is/are rejected.

7)☐ Claim(s) ____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *12 January 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Continuation of Disposition of Claims: Claims pending in the application are 1, 2, 9,11-17,19, 20, 22, 28-36, 38, 39, 41, 47, 49-55, 57-60, 66, 68-74 and 76.

DETAILED ACTION

1. Applicant's responses and amendments filed May 1, 2007, July 26, 2007 and September 28, 2007 are acknowledged and entered. Claims 1, 2, 9,11-17,19, 20, 22, 28-36, 38, 39, 41, 47, 49-55, 57-60, 66, 68-74 and 76 are pending. Claims 11-14, 30-33, 49-52 and 68-71 are withdrawn from consideration being drawn to non-elected subject matter. Claims 1, 2, 9, 15-17, 19, 20, 22, 28, 29, 34-36, 38, 39, 41, 47, 53-55, 57-60, 66, 72-74 and 76 are under examination.

2. The following objection and rejections are withdrawn:

- The objections to claims 9, 20-22, 28, 34, 35, 38, 39, 54, 55 and 72-74 are withdrawn in view of Applicant's amendment.
- The rejection of claims 19, 38, 57, 76 and 95 under 35 U.S.C. 101 is withdrawn in view of Applicant's amendment.
- The rejection of claims 39, 41, 47, 53-55, 57-60, 66, 72-74 and 76 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, is withdrawn in view of Applicant's amendment.
- The rejection of claims 3, 21, 40, 59 and 60 under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an antibody comprising a variable light chain comprising SEQ ID NO: 4 that binds Dengue NS-1, does not reasonably provide enablement for an antibody comprising a variable light chain comprising SEQ ID NO: 4 that binds any non-NS1 Dengue NS protein, is withdrawn in view of Applicant's amendment.

- The rejection of claims 58-60 and 66 under 35 U.S.C. 102(b) as being anticipated by Valdés *et al.* (*Clinical and Diagnostic Laboratory Immunology*, 2000, 7(5):856-857, "Valdés") is withdrawn because the claims are now directed monoclonal antibodies. Valdés discloses human Dengue antibodies against structural and nonstructural proteins, including antibodies against NS1 (abstract), however, monoclonal antibodies are not disclosed.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 16, 17, 29, 35, 36, 54, 55, 73 and 74 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for antibodies for diagnostic uses in humans, does not reasonably provide enablement for antibodies that impart a therapeutic benefit to a human (pharmaceutical uses in humans). The specification also fails to enable a composition comprising a prophylactically effective amount of at least one compound or protein listed in claim 29. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Applicant's argument has been carefully considered but fails to persuade. Applicant notes that the instantly rejected claims are drawn to compositions, not therapeutic methods, or method of treating/preventing dengue virus infections. Applicant asserts that the recitation of

"therapeutic" or "pharmaceutical use" are not elements of the claimed composition, rather a potential use. Applicant argues that the question of enablement for the rejected claims is whether one would be able to make and use the claimed compositions in view of the disclosure. Applicant asserts that one of skill in the art would be able to make and use the claimed antibodies.

In response to Applicant's remarks, the Office agrees that the question of enablement for the rejected claims is whether one would be able to make and use the claimed compositions in view of the disclosure. As Applicant has stated, the intended use of the composition is not a structural feature of the composition itself. The claimed composition is an antibody that has the ability to impart therapeutic benefit, as indicated in the claims (pharmaceutical uses). Because Applicant has included an intended property (use) of the claimed composition, the Office must ask the question whether one of skill in the art is capable of making and using the composition that has the ability to impart therapeutic benefit. It is with this understanding that the claims have been rejected. If Applicant were to amend the claims to remove the language in question, the rejection would be withdrawn. However, the functional use of the claimed product recited in the claims cannot be ignored for purposes of 35 U.S.C. 112, first paragraph.

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 58-60, 66, 72-74 and 76 are rejected under 35 U.S.C. 102(b) as being anticipated by Flamand *et al.* (WO 00/75665 A1, the English translation will be referenced, U.S. Patent 6,870,032 B1, "Flamand"). The claims are drawn to isolated monoclonal mammalian anti-Dengue virus antibodies and a composition thereof. The monoclonal antibodies bind to the same region of a Dengue virus protein as an antibody comprising at least one light chain CDR of SEQ ID NO: 4. (Note that the structural components of the claims are addressed, not the non-enabled embodiments referred to in the rejection above). An antibody comprising SEQ ID NO: 4 binds NS-1. Also claimed are articles of manufacture and devices comprising the antibodies. Also claimed are isolated populations of monoclonal mammalian antibodies produced by a method comprising providing a host that expresses, in recoverable amounts, said antibodies.

Flamand discloses assays for diagnosing Flavivirus infection using antibodies with high affinity for NS1 protein in its hexameric form (soluble form). Flamand's monoclonal antibodies (populations) bind Dengue NS1 (col. 4, lines 24-62). The antibodies are disclosed as suitable for use as immunogenic compositions further comprising pharmaceutically acceptable vehicles (col. 7, lines 17-25 and 48-53). Since Flamand discloses that the antibodies can be used for passive immunization, one would expect that the route of administration would be oral, intravenous, or any other suitable route. With regard to the limitation that the container be suitable for various routes of delivery, the containers in which the antibodies are held, presumably vials, are suitable for delivery via the following routes: bolus, vaginal, rectal, buccal and sublingual. The antibodies are packaged in a kit or boxed set for diagnostic purposes, which necessarily contain containers comprising the antibodies (articles of manufacture), packaging materials, and pharmaceutically acceptable vehicles.

With regard to the method by which the monoclonal mammalian antibodies are produced (host cells, etc.), the method of production of the antibodies is not given patentable weight since the claims are drawn to products. Regardless of the method of production, the antibodies of Flamand and the antibodies instantly claimed are expected to be the same product structurally. Since Flamand's antibodies bind Dengue NS-1, the limitations of the claims have been met. Therefore, the claimed subject matter is taught by Flamand.

Applicant's arguments have been carefully considered but fail to persuade. Applicant asserts that the claimed antibodies are monoclonal, and thus have the same binding specificity as the reference monoclonal antibody. Applicant argues that the specificity of a monoclonal antibody refers to the ability of the antibody to specifically recognize an epitope of an antigen, not merely the ability of the antibody to recognize an antigen. Applicant asserts that two monoclonal antibodies may bind to the same protein, but not have the same specificity because they recognize two different epitopes on the antigen. Applicant also asserts that when a given antigen is used to product monoclonal antibodies, a great number of antibodies with different specificities and varying affinities could potentially be generated. Applicant reasons that there is no evidence that the monoclonal antibodies of Flamand and the monoclonal antibodies of the instant invention bind the same epitope of NS1. Applicant argues that the probability of Flamand's antibodies binding the same epitope bound by the instantly claimed antibodies is extremely low, if not zero, because the NS1 protein has hundreds or thousands of different epitopes against which different monoclonal antibodies recognize.

In response to Applicant's remarks, the Office is aware of the specificity with which monoclonal antibodies bind their respective epitopes. The Office also recognizes that there are

numerous epitopes within NS1 to which monoclonal antibodies may bind, and that two completely different monoclonal antibodies may bind to NS1, but bind to different epitopes. However, because Applicant has chosen to claim the antibodies by their function only and no structure (as in the claims that require the antibody to have SEQ ID NO: 4), the Office is justified in reasonably expecting that the monoclonal antibodies of Flamand are the same as the monoclonal antibodies instantly claimed. Flamand's monoclonal antibodies bind a region of a Dengue virus protein, NS1, which meets the functional limitations provided in the claims. Therefore, the Office has met its burden for demonstrating anticipation.

Conclusion

5. Claims 1, 2, 9, 15, 19, 20, 22, 28, 38, 39, 41, 47, 53 and 57 are allowable.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stacy B. Chen whose telephone number is 571-272-0896. The examiner can normally be reached on M-F (7:00-4:30), alternate Fridays off,. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

/Stacy B. Chen/ 12-13-2007
Primary Examiner, TC1600